

Exhibit 1

REPORTE DE BUSQUEDA INTERNACIONAL

Número de Solicitud Internacional:
PCT/US00/23242

A: CLASIFICACIÓN DEL ASUNTO
CIP (7): A61K 39/02, 39/112
CLASES EUA: 424/200.1, 234.1, 258.1

De conformidad con la Clasificación Internacional de Patentes (CIP) o de conformidad tanto con la Clasificación Nacional como con la Clasificación Internacional de Patentes.

B. CAMPOS BUSCADOS

Documentación mínima buscada (sistema de clasificación seguido de los símbolos de clasificación)
CLASES EUA: 424/200.1, 234.1, 258.1

Documentación buscada otra que la documentación mínima en la medida en que tales documentos están incluidos en los campos buscados: -

Base de datos electrónica consultada durante la búsqueda internacional (nombre de la base de datos y, eventualmente, términos de búsqueda empleados):

MEDLINE, WEST

C: DOCUMENTOS CONSIDERADOS RELEVANTES

Categoría *	Cita de Documento, con indicación, en su caso, de las partes relevantes	Relevante para la Reivindicación Número
X	US 6,080,849 (BERMUDES et al.) 10 de Septiembre de 1997 (10.09.1997), todo el documento, especialmente columna 13.	1,9,12,14,25,26,33,36,38,71,82,84
X	WO 96/40238 (PAWELEK et al.) 19 de Diciembre de 1996 (19.12.1996), páginas 1, 147-156	1,9,12,14,25,36,38,71,82,84
X	PAWELEK et al. "Tumor Targeted Salmonella as a Novel Anticancer Vector", Cancer Research. Vol. 57, Octubre de 1997, artículo completo	1,9,12,14,25,36,38,71,82,84
X ---	LOW et al. "Lipid A mutant Salmonella with suppressed virulence and TNFA induction retain tumor-targeting in vivo". Nature Biotechnology, Vol. 17, Enero de 1999, todo el documento.	1,9,12,14,25,36,38,71,82,84
Y	ver página 39, segunda columna	2
Y	MARR et al. "Tumor immunotherapy using an adenoviral vector expressing a membrane-bound mutant of murine TNF alpha". Gene Ther. Vol. 4, No. 11, Noviembre de 1997 resumen solamente	3,4,27,28,73,74

(X) Se listan documentos adicionales en la continuación del cuadro C.

() Se listan miembros de familia de Patentes en anexo.

* Categorías especiales de documentos citados:

"A" Documento que define el estado general de la técnica que no se considera de relevancia particular.

"E" Documento anterior pero publicado en la fecha de presentación Internacional o después de dicha fecha.

"L" Documento que puede poner en duda la(s) reivindicación(es) de prioridad o que se cita para establecer la fecha de publicación de otra cita o por otra razón especial (según especificación).

"O" Documento que se refiere a una presentación oral, uso, exhibición, u otros medios.

"P" Documento publicado antes de la fecha de presentación internacional pero después de la fecha de prioridad reclamada.

"T" Documento posterior publicado después de la fecha de presentación internacional o de la fecha de prioridad y que no entra en conflicto con la solicitud pero citado para entender el principio o la teoría subyacente de la invención.

"X" Documento de relevancia particular: la invención reclamada no puede ser considerada novedosa o no puede considerarse como incluyendo un paso de invención cuando el documento se toma solo.

"Y" Documento de relevancia particular: la invención reclamada no puede considerarse como incluyendo un paso de invención cuando el documento se combina con uno o varios otros documentos de este tipo, tal combinación siendo evidente para un experto en la materia.

"G" Documento miembro de la misma familia de patentes.

Fecha de Terminación Real de la Búsqueda Internacional: 04 de Noviembre de 2000 (04.11.2000)	Fecha de Envío por Correo del Reporte de Búsqueda Internacional: 12 DE ABRIL DE 2001
Nombre y Dirección Postal de la Autoridad de Búsqueda Internacional/EUA Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Fax No.: (703) 305-3230	Oficial Autorizado: Gary Nickol No. Telefónico: 703-308-0196

Formato PCT/ISA/210 (segunda hoja) (Julio de 1998)

REPORTE DE BUSQUEDA INTERNACIONAL

Número de Solicitud Internacional:

PCT/US00/23242

Cuadro I: Observaciones cuando no se pudieron buscar algunas reivindicaciones (Continuación del elemento 1 de la primera hoja)

Este Reporte de Búsqueda Internacional no ha sido establecido en relación con algunas reivindicaciones de conformidad con el Artículo 17(2) (a) por las siguientes razones:

1. () Reivindicaciones No.:

Porque se relacionan a una materia que no requiere de búsqueda por parte de esta Autoridad, específicamente: -

2. () Reivindicaciones No.:

Porque se relacionan a partes de la Solicitud Internacional que no cumplen con los requerimientos prescritos en una medida tal que no se puede llevar a cabo una Búsqueda Internacional significativa, específicamente: -

3. () Reivindicaciones No.:

Porque son reivindicaciones dependientes y no están redactadas de conformidad con el segundo y tercer enunciados de la Regla 6.4 (a).

Cuadro II. Observaciones cuando falte la unidad de la invención (Continuación del elemento 2 de la primera hoja)

Esta Autoridad de Búsqueda Internacional encontró numerosas invenciones en esta Solicitud Internacional, de conformidad con lo siguiente:

1. () Puesto que todas las tarifas de búsqueda adicional requeridas fueron pagadas oportunamente por el solicitante, este Reporte de Búsqueda Internacional abarca todas las reivindicaciones buscables.

2. () Puesto que todas las reivindicaciones buscables pudieron buscarse sin esfuerzo que justifique el pago de tarifas adicionales, esta Autoridad no requirió el pago de ninguna tarifa adicional.

3. (X) Puesto que algunas de las tarifas de búsquedas requeridas fueron pagadas oportunamente por el solicitante, este Reporte de Búsqueda Internacional abarca solamente las reivindicaciones para las cuales las tarifas fueron pagadas, específicamente las reivindicaciones No.: 1-12, 14, 16-36, 38, 40-47, 71, 73-74, 82, 84

4. () El solicitante no pagó oportunamente tarifas de Búsqueda adicional requeridas. Por consiguiente, este Reporte de Búsqueda Internacional se restringe a la invención mencionada en primera instancia en las reivindicaciones; dicha invención está cubierta por las reivindicaciones No.:

Reivindicaciones 1-38 (todas parcialmente)

Observación sobre la protesta

() Las tarifas adicionales de búsqueda fueron acompañadas por la protesta del solicitante.

(X) Ninguna protesta acompaña el pago de las tarifas adicionales.

Grupo 30, reivindicación(es) 65-70, se refiere a un método para el tratamiento del cáncer que comprende proteínas de fusión.

Grupo 31, reivindicación(es) 71,73-74,82,84, se refiere a un método para el tratamiento del cáncer que comprende la administración de uno o varios agentes quimioterapéuticos.

Grupo 32, reivindicación(es) 72-74,82,84, se refiere a un método para el tratamiento del cáncer que comprende la administración de uno o varios agentes quimioterapéuticos.

Grupo 33, reivindicación(es) 71,75-76,82,84, se refiere a un método para el tratamiento del cáncer que comprende la administración de uno o varios agentes quimioterapéuticos.

Grupo 34, reivindicación(es) 72,75,76,83,84, se refiere a un método para el tratamiento del cáncer que comprende la administración de uno o varios agentes quimioterapéuticos.

Grupo 35, reivindicación(es) 71,77-78,82,84, se refiere a un método para el tratamiento del cáncer que comprende la administración de uno o varios agentes quimioterapéuticos.

REPORTE DE BUSQUEDA INTERNACIONAL

Número de Solicitud Internacional:
PCT/US00/23242

Grupo 24 (Reivindicación 58)
Grupo 25 (Reivindicación 58)
Grupo 26 (Reivindicación 60)
Grupo 30 (Reivindicación 68)
Grupo 31 (Reivindicación 74)
Grupo 32 (Reivindicación 74)
Grupo 33 (Reivindicación 76)
Grupo 34 (Reivindicación 76)
Grupo 35 (Reivindicación 78)
Grupo 36 (Reivindicación 78)
Grupo 37 (Reivindicación 80)
Grupo 38 (Reivindicación 80)
Grupo 39 (Reivindicación 81)
Grupo 40 (Reivindicación 81)
Grupo 41 (Reivindicación 83)
Grupo 42 (Reivindicación 83)
Grupo 49 (Reivindicación 98)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/23242

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 39/02, 39/112
 US CL : 424/ 200.1, 234.1, 258.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/ 200.1, 234.1, 258.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 MEDLINE, WEST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6,080,849 (BERMUDES et al.) 10 September 1997 (10.09.1997), entire document, esp. column 13.	1,9,12,14,25,26,33,36,38,71,82,84
X	WO 96/40238 (PAWELEK et al.) 19 December 1996 (19.12.1996), pages 1, 147-156	1,9,12,14,25,36,38,71,82,84
X	PAWELEK et al. "Tumor Targeted Salmonella as a Novel Anticancer Vector", Cancer Research. Vol. 57, October 1997, entire article	1,9,12,14,25,36,38,71,82,84
X	LOW et al. "Lipid A mutant Salmonella with suppressed virulence and TNF α induction retain tumor-targeting in vivo". Nature Biotechnology, Vol. 17, January 1999, entire document.	1,9,12,14,25,36,38,71,82,84
Y	see page 39, second column	2
Y	MARR et al. "Tumor immunotherapy using an adenoviral vector expressing a membrane-bound mutant of murine TNF alpha". Gene Ther. Vol. 4, No. 11, November 1997, abstract only.	3,4,27,28,73,74

☒ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

04 November 2000 (04.11.2000)

Date of mailing of the international search report

12 APR 2001

Name and mailing address of the ISA/US

Commissioner of Patents and Trademarks
 Box PCT
 Washington, D.C. 20231
 Facsimile No. (703)305-3230

Authorized officer

G. Nicholas Lawrence
 Gary Nickol

Telephone No. 703-308-0196

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: 1-12, 14, 16-36, 38, 40-47, 71, 73-74, 82, 84

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐

The additional search fees were accompanied by the applicant's protest.

☒

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/23242

Group 13, claim(s) 2,16,26,40, drawn to an attenuated tumor-targeted bacteria comprising one or more primary effector molecules and one or more secondary effector molecules, wherein the secondary effector molecule is a bacteriocin release factor (BRP), operably linked to one or more promoters, wherein said attenuated tumor-targeted bacteria is a facultative aerobe or facultative anaerobe.

Group 14, claim(s) 17,20,22-24,41,44,46,47, drawn to an attenuated tumor-targeted bacteria comprising one or more nucleic acid molecules encoding one or more fusion proteins wherein said fusion protein comprises a signal sequence and an effector molecule.

Group 15, claim(s) 18-24,42-47 drawn to an attenuated tumor-targeted bacteria comprising one or more nucleic acid molecules encoding one or more fusion proteins wherein said fusion protein comprises a ferry peptide and an effector molecule.

Group 16, claim(s) 48,50-51,59,61, drawn to a method for treating cancer comprising administering an attenuated tumor-targeted bacteria comprising one or more primary effector molecules, wherein at least one of the primary effector molecules is a TNF family member, operably linked to one or more promoters, wherein said attenuated tumor-targeted bacteria is a facultative aerobe or facultative anaerobe.

Group 17, claim(s) 49-51,59,61, drawn to a method for treating cancer comprising administering an attenuated tumor-targeted bacteria comprising one or more primary effector molecules and one or more secondary effector molecules, wherein at least one of the primary effector molecules is a TNF family member, operably linked to one or more promoters, wherein said attenuated tumor-targeted bacteria is a facultative aerobe or facultative anaerobe.

Group 18, claim(s) 48,52-53,59,61, drawn to a method for treating cancer.

Group 19, claim(s) 49,52-53,59,61, drawn to a method for treating cancer.

Group 20, claim(s) 48,54-55,59,61, drawn to a method for treating cancer.

Group 21, claim(s) 49,54-55,59,61, drawn to a method for treating cancer.

Group 22, claim(s) 48,56-57,59,61 drawn to a method for treating cancer.

Group 23, claim(s) 49,56-57,59,61, drawn to a method for treating cancer.

Group 24, claim(s) 48,58-59,61, drawn to a method for treating cancer.

Group 25, claim(s) 49,58-59,61, drawn to a method for treating cancer.

Group 26, claim(s) 49,60-61, drawn to a method for treating cancer.

Group 27, claim(s) 48,62, drawn to a method for treating cancer.

Group 28, claim(s) 49,63, drawn to a method for treating cancer.

Group 29, claim(s) 64,67,69-70, drawn to a method for treating cancer comprising fusion proteins.

Group 30, claim(s) 65-70, drawn to a method for treating cancer comprising fusion proteins.

Group 31, claim(s) 71,73-74,82,84, drawn to a method for treating cancer comprising administering one or more chemotherapeutic agents.

Group 32, claim(s) 72-74,82,84, drawn to a method for treating cancer comprising administering one or more chemotherapeutic agents.

Group 33, claim(s) 71,75-76,82,84, drawn to a method for treating cancer comprising administering one or more chemotherapeutic agents.

Group 34, claim(s) 72,75-76,83,84, drawn to a method for treating cancer comprising administering one or more chemotherapeutic agents.

Group 35, claim(s) 71,77-78,82,84, drawn to a method for treating cancer comprising administering one or more chemotherapeutic agents.

INTERNATIONAL SEARCH REPORT

Int'l application No.

PCT/US00/23242

Group 24 (Claim 58)
Group 25 (Claim 58)
Group 26 (Claim 60)
Group 30 (Claim 68)
Group 31 (Claim 74)
Group 32 (Claim 74)
Group 33 (Claim 76)
Group 34 (Claim 76)
Group 35 (Claim 78)
Group 36 (Claim 78)
Group 37 (Claim 80)
Group 38 (Claim 80)
Group 39 (Claim 81)
Group 40 (Claim 81)
Group 41 (Claim 83)
Group 42 (Claim 83)
Group 49 (Claim 98)

PCT

From the INTERNATIONAL BUREAU

**NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES**

(PCT Rule 47.1(c), first sentence)

To:

BALDWIN, Geraldine, F.
Pennie & Edmonds LLP
1155 Avenue of the Americas
New York, NY 10036
ETATS-UNIS D'AMERIQUE

PENNIE & EDMONDS
RECEIVED

APR 26 2001

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1 o.k. for filing

IMPORTANT NOTICE

Date of mailing (day/month/year) 12 April 2001 (12.04.01)			
Applicant's or agent's file reference 8002-059-228			
International application No. PCT/US00/23242	International filing date (day/month/year) 24 August 2000 (24.08.00)	Priority date (day/month/year) 04 October 1999 (04.10.99)	
Applicant VION PHARMACEUTICALS, INC. et al			

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
AU,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
AE,AG,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,BZ,CA,CH,CN,CR,CU,CZ,DE,DK,DM,DZ,EA,EE,EP,ES,
FI,GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,
MN,MW,MY,MZ,NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU.
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 48.1(a-bis)).
3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
12 April 2001 (12.04.01) under No. WO 01/25397

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. (41-22) 740.14.35</p>	<p>Authorized officer J. Zahra</p> <p>Telephone No. (41-22) 338.83.38</p>
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JUL 24 2001

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REFERRED TO-M

O.K. for filing

From the INTERNATIONAL BUREAU

INFORMATION CONCERNING ELECTED
OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

BALDWIN, Geraldine, F.
Pennie & Edmonds LLP
1155 Avenue of the Americas
New York, NY 10036
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 12 July 2001 (12.07.01)		
Applicant's or agent's file reference 8002-059-228		
IMPORTANT INFORMATION		
International application No. PCT/US00/23242	International filing date (day/month/year) 24 August 2000 (24.08.00)	Priority date (day/month/year) 04 October 1999 (04.10.99)
Applicant VION PHARMACEUTICALS, INC. et al		

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

EP : AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

National : AU, BG, CA, CN, CZ, DE, IL, JP, KP, KR, MN, NO, NZ, PL, RO, RU, SE, SK, US

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

AP : GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW

EA : AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

OA : BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

National : AE, AG, AL, AM, AT, AZ, BA, BB, BR, BY, BZ, CH, CR, CU, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IN, IS, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MW, MX, MZ, PT, SD, SG, SI, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

3. The applicant is reminded that he must enter the "national phase" before the expiration of 30 months from the priority date before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing, if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

The entry into the European regional phase is postponed until 31 months from the priority date for all States designated for the purposes of obtaining a European patent.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer:

Pascal Pizlou

Telephone No. (41-22) 338.83.38

